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CYTOCHROME 2C19 POLYMORPHISM AND RESPONSE TO ADJUNCTIVE CILOSTAZOL VERSUS HIGH MAINTENANCE-DOSE CLOPIDOGREL IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

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Background: Carriage of cytochrome(CYP) 2C19 mutant allelle decreased response to clopidogrel. Although adjunctive cilostazol to dual antiplatelet therapy intensifies platelet inhibition, it remains unknown whether adjunctive cilostazol can overcome the loss-of-function effect of the CYP2C19 polymorphism.

Methods: The CYP2C19 genotyping was performed in 134 patients undergoing elective PCI. After assessment of preprocedural platelet reactivity (PR), patients were randomly assigned to receive either adjunctive cilostazol 100mg twice daily (triple group;n= 69) or high maintenance-dose (MD) clopidogrel of 150 mg/day (high-MD group;n= 65). PR was assessed immediately before procedure and after 30-day therapy by conventional aggregometry and VerifyNow. Primary end point was absolute change of ADP-induced maximal PR (PRmax). High post-clopidogrel PR (HPPR) was defined as PRmax ≥ 50% with 5uM ADP.

Results: In non-carriers of CYP2C19 varinat, the triple group (n= 22) showed similar reductions of PR compared to the high-MD group (n= 22). After 30-day therapy, the rate of HPPR also did not differ between the triple versus high-MD group (4.5% vs. 13.6%, P = 0.300). In carriers of at least one CYP2C19 mutant allelle, changes of 5 or 20 uM ADP-induced PRmax were significantly higher in the triple (n= 47) versus high-MD group (n= 43) (25.8 ± 16.8% vs. 11.1 ± 19.8%, P < 0.001; 26.3 ± 16.0% vs. 11.5 ± 16.3%, P < 0.001, respectively). Likewise, changes of ADP-induced late PR were consistently greater in the triple versus high-MD group. Change of P2Y12 reaction unit in the triple group showed enhanced platelet inhibition than that of the high-MD group (105 ± 75 vs. 64 ± 76, P = 0.012). After 30-day therapy, fewer patients in the triple group had HPPR compared to the high-MD group (6.4% vs. 37.2%, P = 0.001).

Conclusions: Among patients with the CYP2C19 mutant allele undergoing elective PCI, adjunctive cilostazol enhances platelet inhibition and reduces the rate of HPPR than high-MD clopidogrel.